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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/555,865	08/25/2006	**Manuel Sarasa Barrio**	105090.61194US	6865

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EXAMINER	
BALLARD, KIMBERLY	
ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/555,865	SARASA BARRIO, MANUEL	
	Examiner	Art Unit	
	KIMBERLY A. BALLARD	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *5 and 8-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 7, 2011 has been entered.

Status of Application, Amendments and/or Claims

2. Claims 1, 4, 6 and 7 have been amended as requested in the response filed January 7, 2011. Following the amendment, claims 1-19 are pending in the present application.

3. Claims 5 and 8-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 4, 2009.

4. Claims **1-4** and **6-7**, drawn to the extent of the peptides of SEQ ID NO: 2 and SEQ ID NO: 3, are under examination in the current office action.

Withdrawn Rejections

5. The rejection of claims 1-4, 6 and 7 under 35 U.S.C. 112, first paragraph (enablement), set forth at paragraph 6 of the previous office action (mailed 07/07/2010), is withdrawn in view of Applicant's amendments to the claims.

6. The rejection of claims 6 and 7 under 35 U.S.C. 102(e) as being anticipated by US 2006/0188512 A1 by Yednock et al. is withdrawn in view of Applicant's arguments and upon further consideration by the examiner. Yednock excludes the use of a peptide consisting of Aβ33-42 (i.e., the instant SEQ ID NO: 3) for therapeutic immunization, and does not explicitly teach the peptide of Aβ33-40.

Maintained Rejections

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/72880 A2 by Schenk et al. (published December 7, 2000; reference AM on IDS

filed 11/07/2005). The rejection is maintained for reasons of record and as discussed below.

Response to Arguments

9. In the response filed January 7, 2011, Applicant points to Table 5 at p. 67 of the Schenk document and asserts that the Aβ33-42 peptide (SEQ ID NO: 3 of the instant invention) is not capable of stimulating an immune response. Applicant therefore argues that the activity of Aβ33-42 (i.e., SEQ ID NO: 3) as an immunogen is not taught by Schenk because Schenk demonstrates that this peptide was unable to trigger an immune response in animals. Further, Applicant argues that there is no teaching that a peptide of SEQ ID NO: 2 (i.e., Aβ33-40) would serve as an immunogen. Therefore, Applicant alleges that Schenk fails to teach each and every element of the present invention as claimed.

10. Applicant's arguments have been fully considered but they are not persuasive. Contrary to Applicant's assertions, Table 5 does not indicate or suggest that the peptide of Aβ33-42 would not serve as an appropriate immunogen for therapeutic purposes. Quite the opposite, the Table describes whether or not T-lymphocytes obtained from animals immunized with the various Aβ peptide immunogens proliferate in when stimulated with Aβ1-40 peptide. In other words, it shows whether immunization with the various peptides elicited an inappropriate T-cell response against Aβ1-40. Thus, in this assay a score of zero (as in no responders) is a desirable thing.

Further, as was indicated previously, Schenk teaches that immunogenic fragments of Aβ include those with a length of 8 contiguous residues (see p. 14, lines

30-32). Schenk also teaches any of the different naturally occurring forms of Aβ, including Aβ39, Aβ40, Aβ41, Aβ42 and Aβ43, are included as part of the invention (see p. 14, lines 9-10). Thus, in general any 8-amino acid immunogenic fragment of these peptides, such as any 8-amino acid sequence of the Aβ40 peptide, is encompassed by the teachings of Schenk. In particular, Schenk discloses the peptide of Aβ33-42 as well as the peptides of Aβ35-40 and Aβ35-42. Because Aβ40 and Aβ42 are the most prevalent forms of the Aβ peptide, it is reasonable to conclude that a peptide of Aβ33-40, which is an Aβ fragment of 8 amino acids, is also implicitly included within the teachings of Schenk. Accordingly, the rejection of claims 1-4, 6 and 7 is maintained.

11. Claims 1-4 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2006/0188512 A1 by Yednock et al. (published August 24, 2006; priority to February 1, 2003). The rejection is maintained for reasons of record and as discussed below.

Response to Arguments

12. In the response filed January 7, 2011, Applicant argues that Yednock merely mentions the use of fragments from central or C-terminal regions of Aβ but does not teach a method of treatment of amyloid diseases using, in particular, SEQ ID NO: 2 or 3. In addition, Applicant asserts that Yednock's claim 48 expressly excludes a peptide that would induce antibodies that would specifically bind to an Aβ33-42 or Aβ35-40 peptide, and these peptides are also specifically excluded for use in the therapeutic method according to Yednock's claim 1. Therefore, Applicant argues that Yednock does not teach a method for treating a disease with peptides of SEQ ID NO: 2 or 3.

13. Applicant's arguments have been fully considered but are not persuasive. Firstly, even though Applicant's elected invention is directed to the therapeutic use of the peptides of SEQ ID NOs: 2 and 3, the broadest reasonable interpretation of the claims (and particularly of claims 1-3) includes the use of any Aβ peptide conjugated to a protein immunogen for the production of anti-Aβ antibodies. Thus, the teachings of Yednock are directly on point to the treatment of Alzheimer's disease in a patient comprising immunizing the patient with an immunogenic Aβ peptide conjugated to KLH, as recited in present claims 1-3.

Secondly, the examiner disagrees with Applicant's statement that Yednock "merely mentions the use of fragments from the central or C-terminal regions of Aβ". Contrary to Applicant's assertion, the therapeutic method disclosed by Yednock can only best be characterized as teaching the use of central or C-terminal regions of Aβ for immunization of subjects. As noted by Applicant, Yednock explicitly teaches that the immunogenic peptides to be administered should generate antibodies that specifically bind to one or more epitopes between residues 12 to 43 of Aβ (i.e., central and C-terminal regions of Aβ) without generating antibodies that specifically bind to one or more epitopes within residues 1-11 of Aβ (i.e., the N-terminal region of Aβ). This disclosure is consistent with embodiments of the presently claimed method. Specifically, it is noted that Yednock teaches that the peptide immunogen Aβ17-24 may be used therapeutically (see [0034] and Yednock's claims 1 and 48). This Aβ peptide is the instant peptide of SEQ ID NO: 1, which although non-elected, is still recited in the

claims (claim 4) and encompassed by the presently claimed invention. Therefore, the teachings of Yednock are still anticipatory for present claims 1-4.

New Objections and Rejections

Claim Objections

14. Claims 4, 6 and 7 are objected to because of the following informalities:

Claim 4 recites "lengthening by addition of amino acid *residue* appropriate..." (emphasis added), which is grammatically awkward. Amendment to "residues" would negate this objection for claim 4.

Claims 6 and 7 have each misspelled the word "residues" as "*resides*" in the last line of each of the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0073655 A1 by Chain (published Apr. 17, 2003).

Chain discloses a method of treating a subject having Alzheimer's disease comprising administering an antibody that is free end-specific for the C-terminus of Aβ. Chain teaches that the most effective target for end-specific antibodies as therapy for Alzheimer's disease is likely to be Aβ40, which forms the bulk of circulating amyloid b peptide, or the more toxic but less abundant Aβ42 or Aβ43 species that can seed amyloid deposition (see [0041]). In particular, the use of antigenic sequences such as Aβ33-40 and Aβ33-42, to which the free end-specific antibodies should be targeted to, is disclosed at paragraph [0076]. For example, Chain discusses that the free end specific antibody is targeted to amino acids 33-40 of the C-terminus-truncated Aβ peptide. Further, Chain notes that Aβ1-40 peptide serves as a representative example; the same fragments can be derived from Aβ1-42, which would give the epitope of Aβ33-42.

Chain teaches that for the production of antibodies, humans may be immunized by injection with the relevant epitope or with any fragment or oligopeptide thereof, which as immunogenic properties (see [0082]). For the design of immunogenic peptides, Chain discloses that a cysteine residue can be added to the end of the above immunogenic peptides to facilitate coupling to a carrier protein, such as keyhole limpet hemocyanin (KLH) (see [0080]). These teachings address specifically recited

limitations of conjugation of the Aβ peptide to a protein immunogen in claims 1 and 3, and lengthening by addition of amino acid residue appropriate for conjugating the protein immunogen to the Aβ peptide, as in claims 4, 6 and 7.

It would have been obvious to one of ordinary skill in the art at the time the invention was filed to modify Chain's disclosed therapeutic method of passive immunization, comprising administration of antibodies, by instead actively immunizing a patient by administering an antigenic peptide of Aβ conjugated to an immunostimulatory protein for the treatment of Alzheimer's disease, wherein the Aβ peptide is Aβ33-40 or Aβ33-42. Chain teaches that free end-specific antibodies directed such epitopes of Aβ are useful for the treatment of Alzheimer's disease, and further teaches various immunization procedures including conjugating the desired Aβ peptide fragment to KLH to induce an antibody response, such as in humans. The ordinarily skilled artisan would have been aware that both active (administration of antigen) and passive (administration of antibodies) immunization techniques have been used for immunotherapy of Alzheimer's disease (as evidenced, for example, by the Schenk and Yednock references discussed above), and therefore it would have been obvious to the ordinarily skilled artisan to use of a specific peptide immunogen conjugate to elicit a specific antibody response for therapy of AD. This is because the artisan has good reason to pursue the known options within his or her technical grasp to obtain predictable results. Particularly in view of Chain's teachings on the use of immunogenic Aβ peptide constructs for generating an appropriate antibody response, such would have amounted to simple substitution of one known element (i.e., active immunization

with peptide immunogens) for another (i.e., passive immunization with antibodies) to yield predictable results. Accordingly, the teachings of Chain render obvious the presently recited invention of claims 1-4, 6 and 7.

Conclusion

17. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is (571)272-2150. The examiner can normally be reached on Monday-Friday 8:30 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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